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14. ABSTRACT- Spinal cord injury (SCI) is frequently accompanied by traumatic brain injury (TBI), but evidence-based approaches for treatment of this "dual-diagnosis" are lacking. This project proposed using current clinical-practice evidence to guide development of an animal model to provide a new tool for studying the biological mechanisms involved, and to open new directions for therapeutics for combined injury. During this second year, we have focused on building a clinical TBI+SCI patient database from the Santa Clara Valley Medical Center and from the VAPAHCS, that details the acute and chronic stages of recovery after dual-injury. This required development of common data elements and methods for querying different types of patient records. We now have an overview of recovery and the medications given to the SCI+TBI patients, and have tracked the duration of all medications prescribed during admission for acute rehabilitation. More medications are used in the dual-diagnosis patients than for each injury alone. We have also built a database of SCI+TBI patients from records at SFGH providing information on acute ICU treatment of SCI+TBI patients. These clinical data are now being used to develop hypotheses to test in the newly established model of SCI+TBI during the last year of the grant.
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Translational Research Partnership

SCI with Brain Injury: Bedside-to-Bench Modeling for Developing Treatment and Rehabilitation Strategies

Progress Report
9/30/2011- 8/31/2012

Initiating Principal Investigator
Michael S. Beattie, Ph.D.
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INTRODUCTION

The goal of this Translational Research Partnership is to gather information on clinical outcomes and practices from several collaborating neurotrauma programs and synthesize this information to inform the development of relevant animal models of the dual diagnosis of Spinal Cord Injury (SCI) and Traumatic Brain Injury (TBI). These models will be used to identify improved therapeutic strategies that can be tested in the clinical setting. The process is meant to be iterative and interactive, producing a "community of practice and research."

The project links the Brain and Spinal Injury Center at the University of California, San Francisco (UCSF) with the Spinal Cord Injury and Brain Injury units at the Santa Clara Valley Medical Center (SCVMC) and the VA Palo Alto Health Care System (VAPAHCS).

In the first annual report, we reported that teleconferencing systems were established to facilitate communication among the study sites, and all Investigators participated in a series of meetings which rotated between participating medical centers to develop clinical database search strategies. These strategies allowed us to synthesize a dual diagnosis database, which we report in more detail below.

BODY

In the text below, we have taken the Statement of Work as a template and detailed how each task was completed and milestones accomplished.

Specific Aim 1: Develop community of practice and research and focus groups; and develop clinical database search strategy and dual diagnosis data

Task 1: Continue development of community of practice and research and focus groups

1a. All Investigators' meetings

The Principal and Partnering Investigators have continued to meet to develop the community of practice and research linking the basic scientists working on animal models of brain and spinal cord injury with the clinical scientists working with patients having spinal cord injuries and traumatic brain injuries. During the second year of the project, this community has continued to develop and has grown to include several new members. Face-to-face meetings have been held at the VAPAHCS and UCSF as described below.

1b. Teleconference set up

Telephone and internet-based audio conferencing has been set up to facilitate collaboration and reduce the amount of time spent in traveling between institutions in different parts of the Bay Area. WebEx software has been used to allow multicast audio.

1c. Teleconferences

Telephone conferences have been held twice a month on average (see KEY RESEARCH ACCOMPLISHMENTS).

Milestones:

Focus Groups (FG) have continued to be conducted at major national and international conferences.

- Combined conference of International Spinal Cord Society and American Spinal Injuries Association, Washington, DC, 2011
  Meeting of Drs. Beattie, Creasey and McKenna with Dr. Fin Biering-Sorensen, President of International Spinal Cord Society, regarding Common Data Elements which he has championed internationally. Focus group with hand therapists from Cleveland Ohio and VA Palo Alto. Participation in symposium on Common Data Elements.
- American Spinal Injuries Association, Denver, Colorado 2012
  Meeting of Drs. Beattie, McKenna and Creasey with Dr. Sukvinder Kalsi-Ryan who developed the Graded and Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) for assessment of hand function, and Lisa Johansen, PhD, RPT, who is using it at VAPAHCS.
- International Spinal Cord Society, London, England, 2012
  Two poster presentations (see Reportable Outcomes)

Task 2: Develop clinical database search strategy

Developing a clinical database search strategy was accomplished in Year One of the grant. For Year Two of the grant, the focus groups recommended review of individual charts of patients to compare their medications at the time of initiation of rehabilitation and at the time of discharge from acute rehabilitation. These trends in medication use and discontinuation will be provided to the animal model group in an effort to model clinical practice from the bedside to bench.

Task 3: Query Dual Diagnosis clinical database

Having reviewed the databases available locally and nationally for SCI and TBI, the Investigators obtained data from the SCI and the TBI Systems of Care at SCVMC, and the SCI Service and the Polytrauma Center at VAPAHCS.

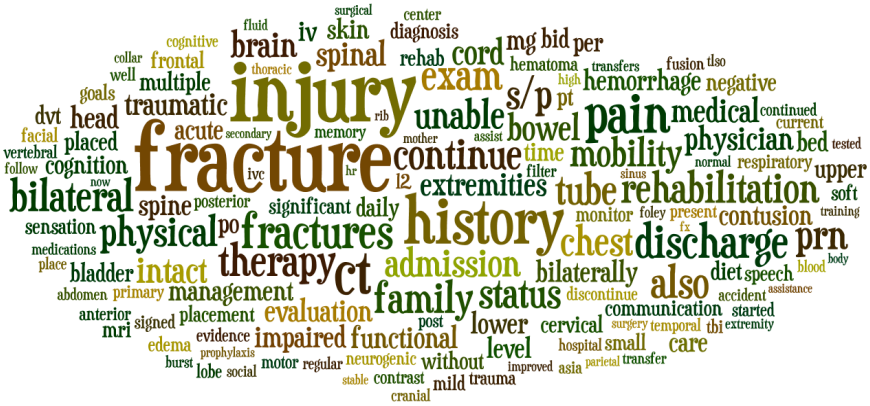
3a1. SCI and TBI Systems of Care at SCVMC

Patients who had undergone TBI rehabilitation at SCVMC between 1989 and 2010 were identified in the TBI Model Systems (TBIMS) National Database when their Form I (enrollment data) also indicated presence of an SCI.

The admission and discharge notes of 14 patients with combined TBI and SCI diagnosis were then extracted from the hospital records of SCVMC and text mined in detail. The text was parsed into a database that was designed to track the treatment and recovery of the patients throughout the time spent in the brain and spinal rehabilitation facility. Once the database was compiled, an initial comparison utilizing a word cloud analysis of admission and discharge notes was used to provide the first broad visualization of the database.

In this word cloud analysis, the larger a word is in size, the more frequently it appears in the document. In the example below, “fracture” appeared in high frequency. We determined that many of the TBI and SCI patients had undergone multiple fractures

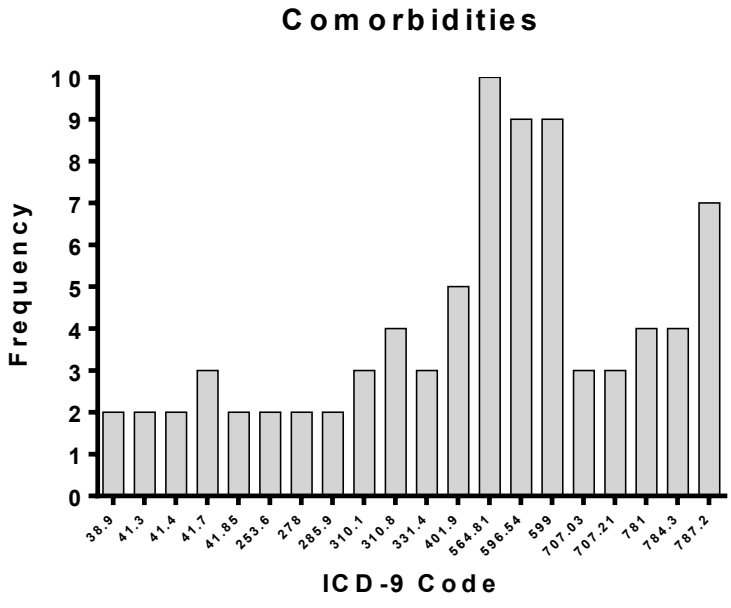
at the time of their injury. This was in keeping the expectation that TBI and SCI patients experience multiple co-morbidities or "polytrauma."



Admission notes:

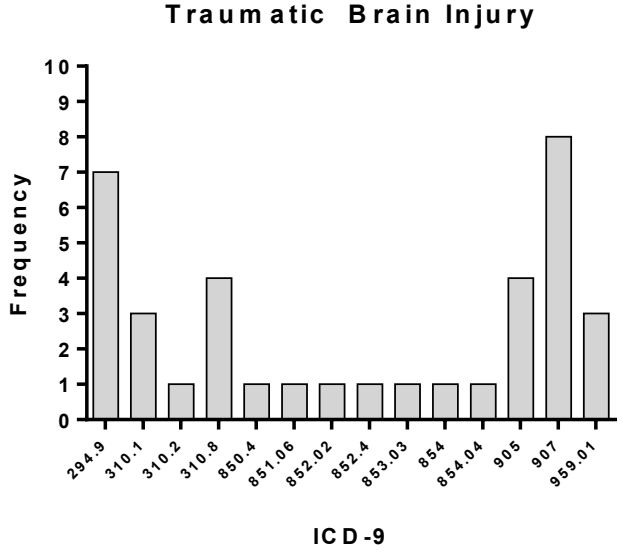
Discharge notes:

The 14 patients with SCI+TBI had a total of 343 unique International Classification of Diseases, Ninth Edition (ICD-9) codes, confirming the variety of comorbidities in this sample. A histogram of the twenty commonest ICD-9 codes for co-morbidities is shown below.

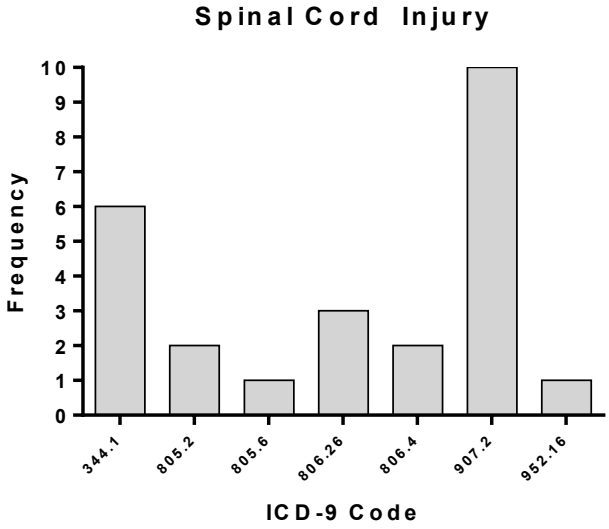


Type	Code	Subject(s)
SEPTICEMIA NOS	38.9	1, 8
K. PNEUMONIAE INFECT	41.3	13, 14
E. COLI INFECTION	41.4	1, 14
PSEUDOMONAS INFECT NOS	41.7	8, 9, 12
GRAM-NEG BACT INFECT NEC	41.85	4, 13
NEUROHYPOPH DISORD NEC	253.6	4, 8
OBESITY NOS	278	4, 9
ANEMIA NOS	285.9	3, 12
PERSONALITY CHANGE CCE	310.1	1, 7, 14
OTH NPMD FOLLOWING OBD	310.8	1,2, 8, 10
OBSTR HYDROCEPHALUS	331.4	1, 4, 8
HYPERTENSION NOS	401.9	1, 4, 8, 11, 13
NEUROGENIC BOWEL	564.81	1, 4, 7, 8, 9, 10, 11, 12, 13, 14
NEUROGENIC BLADDER NOS	596.54	1, 4, 7, 8, 9, 11, 12, 13, 14
URINARY TRACT INF NOS	599	1, 4, 7, 8, 9, 10, 12, 13, 14
PRESSURE ULCER-LOW BACK	707.03	4, 9, 14
STAGE I PRESSURE ULCER	707.21	8, 12, 14
ABN INVOL MOVEMENT NEC	781	3, 8, 12, 14
APHASIA	784.3	8, 11, 12, 13
DYSPHAGIA	787.2	1, 4, 8, 9, 11, 12, 13

ICD-9 codes commonly associated with TBI and SCI respectively were extracted from the hospital records and are shown in the two charts below.



Type	Code	Subject(s)
PERSIST MENT DIS CCE NOS	294.9	1, 3, 4, 6, 8, 12, 13
PERSONALITY CHANGE CCE	310.1	1, 7, 14
POSTCONCUSSION SYNDROME	310.2	1
OTH NPMD FOLLOWING OBD	310.8	1, 2, 8, 10
CONCUSSION-DEEP COMA	850.4	6
CORTEX CONTUSION-NEC	851.06	2
TRAUMATIC SAH-BRIEF	852.02	1
TRAUMATIC EXDH-NOS	852.4	8
OTH TRAUM ICH-MOD	853.03	11
OTH INTRACRANIAL INJURY-NOS	854	4
OTH INTRACRANIAL INJURY-LONG	854.04	6
LATE EFF SKULL/FACE FX	905	8, 11, 12, 13
LATE EFF IC INJURY	907	1, 2, 3, 4, 6, 8, 10, 14
HEAD INJURY NOS	959.01	1, 7, 10



Type	Code	Subject(s)
PARAPLEGIA	344.1	7, 9, 10, 12, 13, 14
FX DORSAL VERTEBRA-CLOSE	805.2	9, 13
FX SACRUM/COCCYX-CLOSED	805.6	1
T7-T12 FX-CL/COMP CRD	806.26	4, 9, 14
CL LUMBAR FX W CORD INJ	806.4	6, 10
LATE EFF SPINAL CORD INJ	907.2	1, 2, 3, 4, 7, 9, 10, 12, 13, 14
T7-T12 COMPL CORD LESION	952.16	7

Patients were coded with a variety of ICD-9 codes, and individual patients were often coded with more than one ICD-9 code for their SCI and also for their TBI. Note that only 13 out of 14 patients had an ICD-9 code that referenced a traumatic brain injury, and only 11 out of 14 patients had an ICD-9 code that referenced a spinal cord injury.

This indicates that using ICD-9 codes to search hospital records for patients with TBI, SCI, and both TBI and SCI is not a sufficient search strategy to identify all such patients. The search strategy actually used to identify these patients identified individuals who would have not have been found merely by searching for appropriate ICD-9 codes.

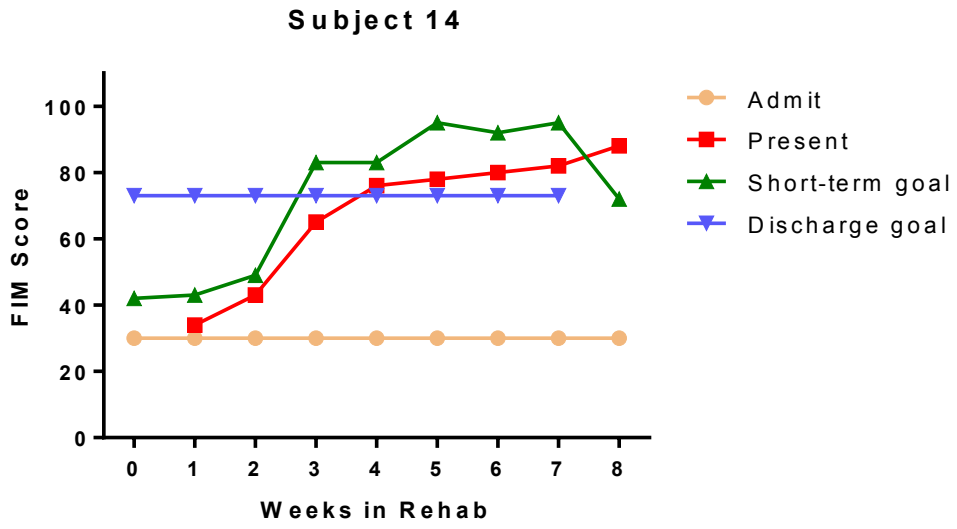
We extracted demographic data of the TBI and SCI patients in the database to provide a targeted analysis that would provide essential information for further hypothesis testing. The analysis below includes age, gender, etiology of injury, number of days until admission into rehab, length of stay in rehabilitation, and Glasgow Coma Scale (GCS). In addition, the database includes data on injury specifics, surgical procedures, diagnostic findings, physical and neurological exam findings, and rehabilitation assessment plans.

Demographics	**Age**		**Gender**		**Etiology**		**# days until rehab admission**		**Rehab LOS**	
Data	Mean	St. Dev	Male	Female	Vehicular	Fall	Mean	St Dev	Mean	St Dev
TBI/SCI (N =14)	33.6	17.1	71.4 %	28.6%	78.6%	21.4 %	29.6	24.4	55.9	39.7

Glasgow Coma Scale	**Mild (13-15)**	**Moderate (9-12)**	**Severe (<= 8)**	**Not Reported**
TBI/SCI (N = 14)	14.29%	7.1%	64.3%	14.3%

In addition, we obtained de-identified Functional Independence Measure (FIM) scores that tracked the functional recovery of the TBI and SCI patients during their stay in rehabilitation. FIM graphs were plotted against the number of weeks spent in rehabilitation. We were able to visualize the functional recovery of each patient throughout rehabilitation. For example, the analysis below shows a single patient with a dual TBI and SCI.

Key: Admit (baseline score recorded at time of admission),
Present (raw score recorded during rehabilitation sessions),
Short-term goal (decided during weekly conference),
Discharge goal (score that is the target for discharge).



Finally, descriptive statistics were performed on the FIM and detailed recovery summaries were obtained.

Descriptive Statistics		Mean		Std. Deviation	Std. Error	Gain/Loss
		Admit	Discharge	Discharge	Discharge	Overall
Self Care	Eating	2	5	1.45	0.51	3
	Grooming	3	5	1.36	0.48	2
	Bathing	1	3	0.96	0.34	2
	Dress Upper	1	4	0.75	0.26	3
	Dress Lower	1	3	1.01	0.36	2
	Toileting	1	3	1.49	0.53	2
	Bladder Level of Accident	2	3	1.91	0.68	1
	Bladder Frequency of Accidents	4	5	1.36	0.48	1
	Bowel Level of Assistance	2	4	2.06	0.73	2
	Bowel frequency of accidents	4	5	1.60	0.56	1
Transfers	Bed, Chair, Wheelchair	1	3	1.34	0.47	2
	Toilet	1	3	1.75	0.62	2
	Tub Transfer	1	2	1.54	0.63	1
	Shower Transfer	0	2	1.90	0.72	2
L.Motion	Walk	0	2	2.08	0.74	2
	Wheelchair	1	4	0.93	0.33	3
	Stairs	0	2	1.73	0.61	2
Social Cognition	Comprehension	3	5	0.94	0.33	2
	Expression	3	5	1.12	0.40	2
	Social Interaction	3	5	1.22	0.43	2
	Problem Solving	2	4	1.16	0.41	2
	Memory	2	4	1.45	0.51	2
FIM Score		29	62	13.57	4.80	33

In summary, the second year succeeded in building a clinical TBI and SCI patient database from the Santa Clara Valley Medical Center models system database that details the acute as well as the chronic stage of recovery. During the third year, we plan to increase the number of patients in the TBI + SCI cohort and develop more detailed analysis of the database.

3a2. SCI Service and the Polytrauma Center at VAPAHCS

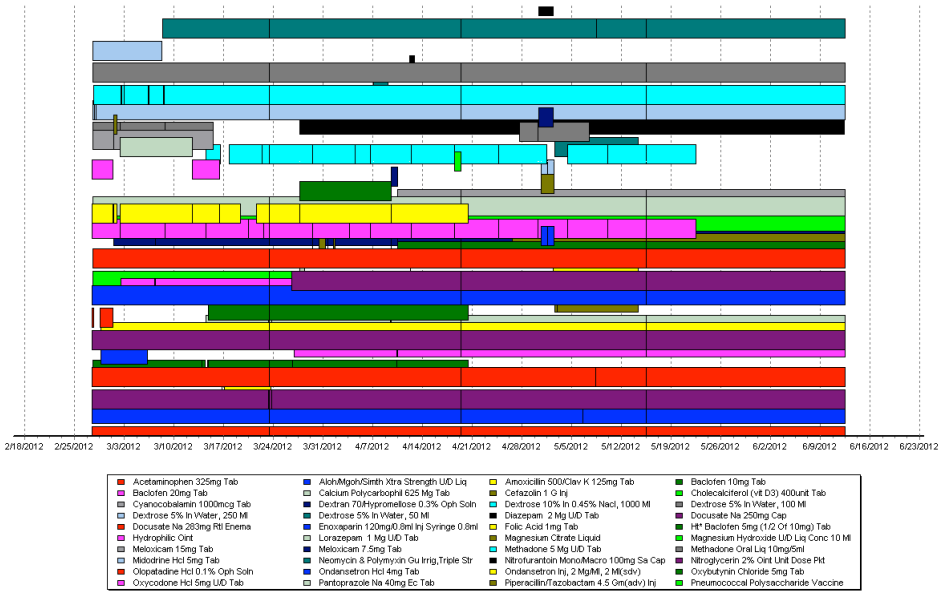
The strategy used with the Santa Clara Valley records was initially used as a model for extracting data on patients with TBI and SCI in the VA Palo Alto Health Care System, but the considerable differences between these two health care systems necessitated different approaches. The Polytrauma Service at VAPAHCS was founded in 2005, unlike the Model TBI System which has been in operation since 1989. As a result, a search of patients admitted for TBI rehabilitation only identified three patients who also had SCI. The records of patients recently admitted to the VA SCI Service for rehabilitation after acute SCI were therefore searched to identify those with TBI. The full text of all notes on these patients were searched for phrases such as “TBI” and “GCS,” and the context of these phrases was examined to determine the way they were used (for example, excluding patients in which the notes recorded that “TBI was ruled out”).

This search strategy showed that of an initial cohort of the 45 patients most recently admitted to the SCI Service for rehabilitation after acute SCI, ten (22%) had a TBI. As with SCVMC, we found that ICD-9 codes did not provide a reliable search strategy for identifying SCI and TBI patients.

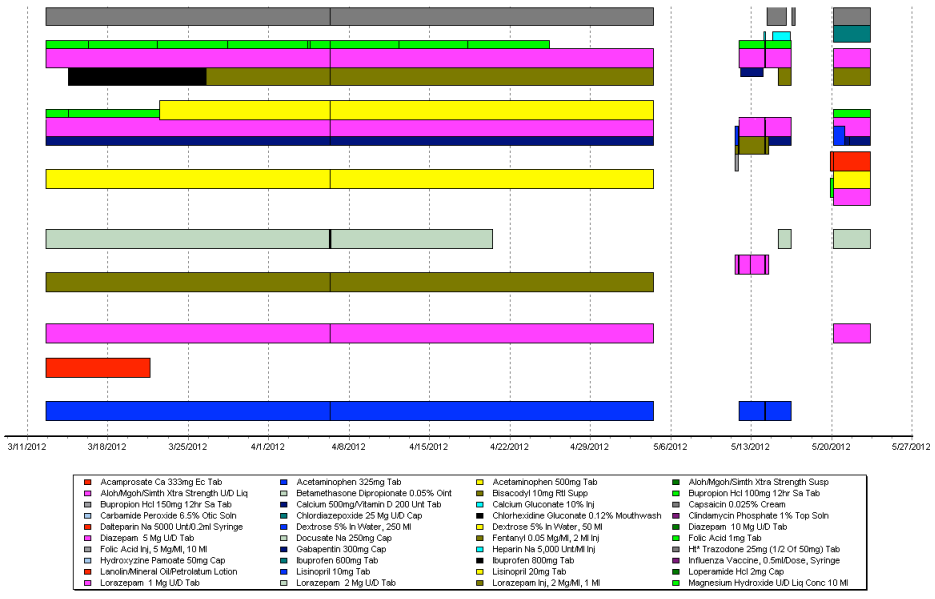
To provide an initial overview of medications we produced a medication cloud that tracked duration of all medications prescribed during admission for acute rehabilitation. A medication cloud is shown for both a SCI patient and a TBI + SCI

patient to provide a brief visualization of medications that were administered and their duration. Note the greater numbers of medications used in the Dual Diagnosis patient. We are planning to use the word cloud analysis to track medication duration during the chronic stage also.

SCI+TBI patient at VA

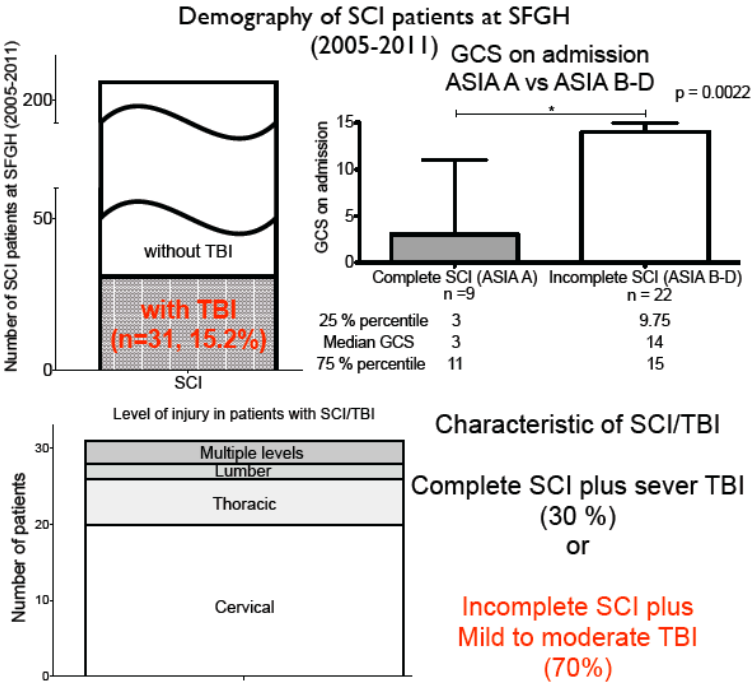


SCI only patient at VA



3a3. Patients at UCSF/SFGH. Under the supervision of Dr. Manley, Dr. Tomoo Inoue has examined the demographics and clinical picture for 203 SCI patients admitted to SFGH from 2005-2012. Of these, 31 were charted as having concurrent TBI. These data were reported, in part, in an abstract presented at the annual Society for

Neuroscience meeting in New Orleans (October, 2012)(Inoue et al, 2012). Patients with complete SCI were more likely to have a lower ASIA score than those with incomplete SCI. The level of injury was predominantly cervical, although a little over a third had thoracic, lumbar or multiple level injuries. Since patients treated at the acute neurotrauma center at SFGH are discharged to rehabilitation centers (including the SCVMC and, rarely, the VAPAHCS, rehabilitation measures are not easily available for this cohort, although we have excellent early data for them. One of the goals is to provide better early care data from the VA and SCVMC cohorts, and better long-term outcome data for the SFGH cohorts. We are currently working on identifying the drugs used in this cohort. We will use these data to plan for prospective studies with follow-up to link what we have learned from this early analysis.



3b. Comparison of SCVMC, VAPAHCS, and SFGH/UCSF

A patient's rehabilitation outcome is greatly influenced by the amount of time that passes before they are admitted for rehabilitation. We determined the number of days between the date of injury and the date of admission into rehabilitation, and also the length of stay in rehabilitation, and compared these between SCVMC and the VAPAHCS hospitals. The analysis is shown below:

Days till Admission to Rehabilitation		
Location	Mean	St Dev
VA (N = 10)	51.5	31.3
SCVMC (N = 14)	29.6	24.4

*No statistically significant difference (T-test)

Length of Stay in Rehabilitation		
Location	Mean	St Dev
VA (N = 10)	96.5	51.4
SCVMC (N = 14)	55.9	39.7

*Statistically significant difference (T-test, p <.05)

Note that the length of stay in rehabilitation is shorter in SCVMC, a civilian hospital, than VAPAHCS, a VA hospital.

The medications provided to Dual Diagnosis patients were compared between these two hospitals. The most common medications prescribed for these patients on admission to rehabilitation at each hospital are shown below:

Admission Medications			
VA	Frequency	SCVMC	Frequency
DOCUSATE	9	DOCUSATE	10
ACETAMINOPHEN	9	ACETAMINOPHEN	7
SENNA	9	SENNA	4
BISACODYL	7	BISACODYL	5
OMEPRAZOLE	7	OMEPRAZOLE	1
ALBUTEROL	6	ALBUTEROL	2
LIDOCAINE	5	LIDOCAINE	1
ASCORBIC ACID	4	ASCORBIC ACID	2
HYDROCODONE/ACETAMINOPHEN	4	HYDROCODONE/ACETAMINOPHEN	2
ONDANSETRON	4	ONDASENTRON	1
ENOXAPARIN	3	ENOXAPARIN	3
GABAPENTIN	3	GABAPENTIN	2
DOXYCYCLINE	3	DOXYCYCLINE	1
LISINOPRIL	3	LISINOPRIL	1
CHLORHEXIDINE	2	CHLORHEXIDINE	2
METOPROLOL	2	METOPROLOL	2
DEXTROSE	2	DEXTROSE	1
MICONAZOLE	2	MICONAZOLE	1
HEPARIN	1	HEPARIN	3
FENTANYL	1	FENTANYL	2
BACLOFEN	1	BACLOFEN	1
FERROUS SULFATE	1	FERROUS SULFATE	1
QUETIAPINE	1	QUETIAPINE	1

Note that the most common medications were those prescribed for management of the neurogenic bowel (e.g docusate, senna, bisacodyl), together with mild analgesics, antacids and bronchodilators.

We compared this with the medications prescribed at the time of discharge from rehabilitation. The most common medications prescribed on discharge are shown below:

Discharge Medications			
VA	Frequency	SCVMC	Frequency
ACETAMINOPHEN	10	ACETAMINOPHEN	7
DOCUSATE	8	DOCUSATE	8
OMEPRAZOLE	8	OMEPRAZOLE	1
SENNA	7	SENNA	4
LIDOCAINE	5	LIDOCAINE	1
ONDANSETRON	5	ONDASETRON	1
GABAPENTIN	4	GABAPENTIN	2
ASCORBIC ACID	4	ASCORBIC ACID	1
BISACODYL	4	BISACODYL	1
TRAZODONE	3	TRAZADONE	5
BACLOFEN	3	BACLOFEN	3
OXYCODONE	3	OXYCODONE	2
LACTOBACILLUS	3	LACTOBACILLUS	1
MICONAZOLE	3	MICONAZOLE	1
FERROUS GLUCONATE	2	FERROUS GLUCONATE	1
SIMVASTATIN	2	SIMVASTATIN	1
METOPROLOL	1	METOPROLOL	1

Note that some bowel medications (docusate and senna) are still among the most commonly prescribed, together with mild analgesics and antacids, but albuterol and low molecular weight heparin have been discontinued and the use of baclofen has increased. The most common medications with potential effects on the central nervous system at the time of admission are shown below.

Medications of Interest
HALDOPERIDOL, OLANZAPINE, RISPERDONE
IBUPROFEN, CELCOXIB, ASPRIN
LEVETIRACETAM, VALPROIC ACID
MODAFINIL, AMANTADINE
CITALOPRAM, BUPROPION
METOCLOPRAMIDE, DROPERIDOL
BACLOFEN
GABAPENTIN
LORAZEPAM
METHADONE
EPOETIN ALPHA
METFORMIN
DOCYCLINE

In the third year of the grant, pilot testing with some of these medications in the combined injury animal model will be undertaken. We will assess gabapentin and baclofen as two of our first drug targets. In addition, we plan to expand the clinical database to allow more detailed comparison of the SCVMC database with the VAPAHCS database so that both can be mined for hypotheses and refined through our community of practice and research.

Specific Aim 2: Develop baseline incomplete SCI plus mild-complicated and moderate TBI rat protocols and outcomes

We have developed an experimental animal model for combined SCI and TBI to help drive mechanistic studies of dual diagnosis. Rats received a unilateral SCI (75 kdyn) at C5 vertebral level, a unilateral TBI (2.0 mm depth, 4.0 m/s velocity impact on the forelimb sensori-motor cortex), or both SCI + TBI. TBI was placed either contralateral or ipsilateral to the SCI. Behavioral recovery was examined using paw placement in a cylinder, grooming, open field locomotion, and the IBB cereal eating test. Over 6 weeks, in the paw placement test, SCI + *contralateral* TBI produced a profound deficit that failed to recover, but SCI + *ipsilateral* TBI dramatically enhanced use of the paw on the SCI side. In the grooming test, SCI + *contralateral* TBI produced worse recovery than either lesion alone even though *contralateral* TBI alone produced no observable deficit. In the IBB forelimb test, SCI + *contralateral* TBI revealed a severe deficit that recovered

in 3 weeks. For open field locomotion, SCI alone or in combination with TBI resulted in an initial deficit that recovered in 2 weeks. Thus, TBI and SCI affected forelimb function differently depending upon the test, reflecting different neural substrates underlying, for example, exploratory paw placement and stereotyped grooming. Concurrent SCI and TBI had radically different effects on outcomes and recovery, depending upon laterality of the two lesions. Recovery of function after cervical SCI was retarded by the addition of a moderate TBI in the contralateral hemisphere, but recovery was markedly enhanced by an ipsilateral TBI. These findings emphasize the complexity of recovery from combined CNS injuries, and the possible role of plasticity and laterality in rehabilitation, and provide a start towards a useful preclinical model for evaluating effective therapies for combine SCI and TBI. This work was performed at SFGH.

Specific Aim 3: Test clinic-driven hypotheses for improving outcomes in the dual diagnosis animal model

Based on the interesting data collected in the experimental model of combined injury showing interactive effects of the SCI and TBI, and the clinical data on drugs used, we are currently working on the experimental design for evaluating effects of gabapentin (used for pain management), baclofen (used for spasticity control), and topiramate (used for controlling seizures). These common treatment targets were all identified in the dual-diagnosis patient populations. Although topiramate has been shown to promote recovery from SCI when delivered in the acute phase (Gensel et al, 2012), it is not known how this treatment given chronically will affect recovery. We hypothesize that this agent will retard recovery if administered chronically, both after SCI and TBI alone, as well as in combined SCI + contralateral TBI. Baclofen has been shown to inhibit recovery after SCI (McDonald et al, 2009), and we hypothesize that the effects will be similar on combined injuries (SCI + TBI contralateral or ipsilateral), as the spinal cord effect will be dominant. Gabapentin may affect cognitive processes after spinal cord injury (McKenna et al, personal communication), and we therefore hypothesize that it will inhibit recovery after combined injury. These studies are being initiated at this time (Oct 2012).

Specific Aim 4: Combine information from clinical practice queries and animal model results to plan for dual diagnosis guidelines

Tasks for Year 3.

KEY RESEARCH ACCOMPLISHMENTS

Specific Aim 1: Develop clinical database search strategy and dual diagnosis data; develop community of practice and research

Task 1. Continue development of community of practice and research focus groups

1a. All Investigators' meetings

- Accomplished February 28, 2012 (SCVMC)
- Accomplished March 9, 2012 (SCVMC)
- Accomplished March 16, 2012 (SCVMC)
- Accomplished March 23, 2012 (SCVMC)
- Accomplished April 13, 2012 (SCVMC)
- Accomplished May 4, 2012 (VAPAHCS)
- Accomplished June 9, 2012 (VAPAHCS)
- Accomplished June 13, 2012 (UCSF)
- Accomplished July 13, 2012 (VAPAHCS)
- Accomplished July 17, 2012 (UCSF)
- Accomplished August 3, 2012 (VAPAHCS)
- Accomplished August 17, 2012 (VAPAHCS)
- Accomplished August 21, 2012 (VAPAHCS)

1b. Teleconference set up

- Accomplished using WebEx Teleconference system

1c. Teleconferences

3/13/2012
4/18/2012
4/20/2012 (During ASIA Conference)
4/24/2012
4/25/2012
5/2/2012 @ UCSF
5/17/2012
8/14/2012

Milestone: Consensus Reports from joint meetings and publication

- Focus group results (Year 1)
- Publication pending (see Specific Aim 4)

Task 2. Develop clinical database search strategy

2a. Model systems

- Existing TBI Model Systems (TBIMS) and SCI Model Systems (SCIMS) national databases identified and local database mined.

2b. VAPAHCS

- Accomplished July 18, 2011

2c. San Francisco General Hospital (SFGH) critical care data

- Accomplished May 31, 2011

2d. Plan for data integration

- Accomplished July 18, 2011

Milestone: Common Data Elements (CDE) focus group; publication pending

- Accomplished July 11, 2011

Task 3. Query Dual Diagnosis clinical database

3a. Query separate databases

- 14 patients from SCVMC TBI Model System Database with Dual Diagnosis identified.
- 31 patients from SFGH Trauma Database identified
- 10 patients from VAPAHCS SCI Database with Dual Diagnosis identified

3b. Merge databases

- Accomplished July, 2012

3c. Query merged databases

- Accomplished July, 2012 and continuing in year 3 (the combined database is currently housed at SFGH and analytic work is being performed there)

3d. Compare focus groups to database results

- Accomplished May 31, 2011, June 30, 2011, July 18, 2011
- Accomplished April 20, 2012, Aug 14, 2012

Milestone: Reports to group & publication pending

- Accomplished May 31, 2011 (at UCSF); June 30, 2011 (at VAPAHCS)

Specific Aim 2: Develop baseline incomplete SCI plus mild-complicated and moderate TBI rat protocols and outcomes

- Accomplished July, 2012 (at UCSF); We have discovered that the interactive effects of SCI+TBI are more complex than we had expected. We have found that cortical lesions can both enhance deficits induced by SCI, but can also facilitate recovery (depending on lesion placement), possibly by disinhibiting suppressive spinal systems affected by the spinal cord injury. Publication of these findings is pending.

Specific Aim 3: Test clinic-driven hypotheses for improving outcomes in the dual diagnosis animal model

- In process; we are currently working on design and implementation of testing in the dual injury animal model, the effects of gabapentin (used for pain management), baclofen (used for spasticity control), and topiramate (used for controlling seizures), all identified as common treatment targets in the dual-diagnosis patient populations.

Specific Aim 4: Combine information from clinical practice queries and animal model results to plan for dual diagnosis guidelines

- Tasks for Year 3

REPORTABLE OUTCOMES

Meetings

Santa Clara Valley Brain Injury Conference, February 24-26, 2011.
"Dual Diagnosis with Brain and Spinal Cord Injury: An Interactive Assessment."

VAPAHCS TBI Research Forum, March 16, 2012
"Combined traumatic brain injury and cervical spinal cord injury in the rat: additive and dissociated effects on neurological outcomes."
Inoue T, Lin A, Ma X, Nout Y, McKenna S, Creasey G, Manley G, Ferguson R, Bresnahan J, Beattie M.

Society for Neuroscience Annual Meeting, New Orleans LA, October 12-17, 2012.
"Combined brain and spinal cord injury: Clinical picture and an animal model."
Inoue T, Lin A, Ferguson A, Creasey G, McKenna S, Manley G, Bresnahan J, Beattie M.

Manuscripts in Preparation

"Interactive Assessment of Dual Diagnosis TBI/SCI Prevalence and Treatment Strategies."

"Combined SCI and TBI: Recovery of forelimb function after unilateral cervical spinal cord injury (SCI) is retarded by contralateral and enhanced by ipsilateral cortical contusion traumatic brain injury (TBI)."
Tomoo Inoue, Amity Lin, Xiaokui Ma, Stephen L. McKenna, Graham H. Creasey, Geoffrey T. Manley, Adam R. Ferguson, Jacqueline C. Bresnahan, and Michael S. Beattie. To be submitted to Experimental Neurology.

CONCLUSION

This project has accomplished its tasks for Years One and Two of a three-year Translational Research Partnership. We have developed a community of practice and research for SCI and TBI in the San Francisco Bay Area of California and conducted focus groups to determine needs and attitudes of clinicians and others to these diagnoses and the potential for modeling the combined diagnosis in animals. We have queried several databases representing veterans and civilians with TBI and SCI and conducted a preliminary merge of clinical databases available for these diagnoses and developed a search strategy for determining the scope of the problem and the areas of priority for animal modeling. On this basis, a rodent model of combined SCI + TBI has been designed and created by the Principal Investigators at the Brain and Spinal Injury Center at UCSF, and has been used to compare the outcomes of SCI, TBI and combined SCI and TBI in this animal model. Ongoing collaboration has been established between the

Principal and Partnering Investigators to interpret the data being obtained, and to define improved outcome measures and treatment practice information based on both the new animal model of combined injury and the merged databases.